Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-36. Cancelled.

37. (Previously presented) A transdermal vaccine, comprising:

(a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent,

the penetrant being in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains;

(b) a compound which specifically has or induces cytokine or anti-cytokine activity; and

(c) an antigen or mixture of different antigens and/or an allergen or mixture of different allergens.

38. (Previously presented) The vaccine of claim 37, wherein the at least two substances are two ionization states or salt forms of the same substance.

39. Canceled.

40. (Previously presented) The vaccine according to claim 37, wherein the less soluble substance with the tendency to aggregate is a polar lipid, and the more soluble substance is a surfactant.

41. (Previously presented) The vaccine according to claim 37, wherein the average diameter of the penetrant is between 30 nm and 500 nm.

42. (Previously presented) The vaccine according to claim 37, wherein the total weight of droplets in the vaccine for use on human or animal skin is 0.01 weight-% (w-%) to 40 w-% of total mass of the vaccine.

43. (Previously presented) The vaccine according to claim 37, wherein total antigen concentration is between 0.001 and 40 w-% of the total penetrant mass.

44. (Previously presented) The vaccine according to claim 37, further comprising a low molecular weight chemical irritant and/or an extract or a compound from a pathogen, or a fragment or a derivative of the chemical irritant, pathogen compound, or extract.

45. (Previously presented) The vaccine according to claim 37, wherein the compound is IL-4, IL-3, IL-2, TGF, IL-6, IL-7, TNF, IL- 1a and/or IL-1b, IL-12, IFN-g, TNF-b, IL-5, IL-10, a type I interferon, IFN-alpha, or IFN-b.

46. (Withdrawn) The vaccine according to claim 37, wherein the compound is an anti-cytokine antibody or an active fragment, a derivative, or an analog thereof.

47. (Previously presented) The vaccine according to claim 37, wherein the antigen is derived from a pathogen.

48. (Previously presented) The vaccine according to claim 47 wherein said pathogen is selected from the group consisting of extracellular bacteria, gram-negative bacteria, gram-positive bacteria, bacteria and viruses, which survive and replicate within host cells, fungi prospering inside host cells, parasites, the causative agent for cholera, Haemophilus species, pathogens triggering paratyphoid, pathogens triggering plague, pathogens triggering rabies, *Clostridium tetani*, pathogens triggering rubella, and pathogens that cause various neoplasiae,

auto-immune diseases or are related to other pathological states of the animal or human body which do not necessarily result from pathogen infections.

49. (Withdrawn) The vaccine according to claim 37, wherein the allergen is of xenogenic or endogenic origin; derived from a microorganism, an animal or a plant; a man made and/or irritating inorganic substance; or a part or component of the human body which was incorrectly processed by or exposed to the body immune system.

50. (Amended) The vaccine according to claim 37, wherein the concentration of ~~each~~ the compound used is up to 1000 times higher than a concentration optimum established in corresponding tests performed by injecting the vaccine or performing the tests in vitro.

51. (Withdrawn) The vaccine according claim 44, wherein the pathogen extract or compound is a lipopolysaccharide, cord-factor, muramyl dipeptide, or an immunologically active part of a membrane of a pathogen; an extract of a pathogen; or bacterial or viral nucleic acids.

52. (Withdrawn) The vaccine according to claim 51, wherein the pathogen extract or compound is a lipopolysaccharide, and wherein the lipopolysaccharide is lipid A or a derivative, modification, or analog thereof.

53. (Withdrawn) The vaccine according to claim 51, wherein the pathogen extract or compound is a lipopolysaccharide, and wherein the lipopolysaccharide is monophosphoryl lipid A.

54. (Withdrawn) The vaccine according to claim 51, wherein the pathogen extract or compound is a lipopolysaccharide, and wherein the lipopolysaccharide is a fatty derivative of saccharose.

55. (Previously presented) The vaccine according to claim 44, wherein the concentration of the compound from a pathogen is between 10 times lower and up to 1000 times higher than the concentration used with the corresponding injected vaccines employing similar antigen.

56. (Withdrawn) The vaccine according to claim 44, wherein the low molecular weight irritant is selected from the classes of allergenic metal ions, acids, bases, irritating fluids, (fatty-) alcohols, (fatty-) amines, (fatty-) ethers, (fatty-) sulphonates, or –phosphates or derivatives or combinations thereof.

57. (Withdrawn) The vaccine according to claim 44, wherein the low molecular weight irritant is a solvent or amphiphile or a derivative or combination thereof

58. (Previously presented) The vaccine according to claim 44, wherein the low molecular weight irritant is selected from the group consisting of surfactants and derivatives and combinations thereof.

59. (Previously presented) The vaccine according to claim 58 wherein the surfactant enhances skin permeation.

60. (Previously presented) The vaccine according to claim 44, wherein the concentration of the low molecular weight irritant is below by at least a factor of 2 to a factor of 10 or more a concentration which is unacceptable owing to local irritation in tests on the same or a comparable subject.

61. (Withdrawn) The vaccine according to claim 37, wherein the allergen is an inhalation allergen, food allergen, drug allergen, contact allergen, injection allergen, invasion allergen, or depot allergen.

62. (Previously presented) The vaccine according to claim 37, wherein the applied dose of the antigen differs by the factor of 0.1 to 100 from the dose which would have to be used with an injection.

63. (Previously presented) The vaccine according to claim 37, wherein the applied dose of an antigen is less than 10 times higher than the dose which would have to be used with an injection.

64. (Previously presented) The vaccine according to claim 37, wherein the applied penetrant dose is between 0.1 mg/cm2 and 15 mg/cm2.

65. (Previously presented) The vaccine according to claim 37, wherein the antigen is a pure or purified antigen.

66. (Previously presented) A kit, comprising at least one dose of the vaccine according to claim 37 in packaged form.

67. (Previously presented) The kit according to claim 66, further comprising at least one injectable dose of an antigen or an allergen.

68. (Withdrawn) A method for generating a protective immune response in a mammal by vaccinating the mammal with a vaccine according to claim 37.

69. (Withdrawn) The method according to claim 68, wherein a suspension of antigen-free penetrants is loaded with the antigen to be associated therewith about 30 minutes before administration of the vaccine.

70. (Withdrawn) The method according to claim 68, wherein the vaccine is applied on skin after pre-treating the skin by an immunoadjuvant manipulation, the manipulation comprising rubbing, pressing, heating, exposing to an electrical or mechanical field, or injecting a non-immunogenic formulation in the skin, wherein such treatment releases immunoadjuvant compounds from the skin or other peripheral immunoactive tissues or reduces the concentration of antagonists to the desired vaccination and/or the duration of action of said antagonists.

71. (Withdrawn) The method according to claim 68 wherein immunogen is applied in a non-occlusive patch.

72. (Withdrawn) The method of claim 68 wherein at least one dose of vaccine is administered.

73. (Withdrawn) The method according to claim 72, wherein the vaccine is administered as a booster vaccination.

74. (Withdrawn) The method according to claim 73, wherein a primary immunization is done invasively and wherein the booster immunization is done non- invasively.

75. (Withdrawn) The method according to claim 68, wherein the vaccine is applied between 2 and 10 times when a non- allergenic antigen is used.

76. (Withdrawn) The method according to claim 75, wherein the time interval between subsequent vaccinations is between 2 weeks and 5 years.

77. (Withdrawn) A method for inducing a protective or tolerogenic immune response comprising administering a vaccine, the vaccine comprising:

(a) a transdermal carrier comprising a penetrant suspended or dispersed in an aqueous solvent,

the penetrant in the form of a minute fluid droplet surrounded by a coating of one or more layers of at least 2 substances that differ by at least a factor of 10 in solubility in a liquid medium,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least 2 substances, the average diameter of homoaggregates of the more soluble substance, or the average diameter of the heteroaggregates of the at least 2 substances, being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance being up to 99 mol-% of the concentration required to solubilize the droplet or corresponding to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least 5 times lower than the elastic deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains;

(b) a compound which specifically has or induces cytokine or anti-cytokine activity; and

(c) an antigen or a mixture thereof and/or an allergen or a mixture thereof.

78. (Withdrawn) The method of claim 77, wherein the vaccine further comprises an extract or a compound from a pathogen or a fragment or a derivative of the pathogen compound or extract.

79. (Withdrawn) The method of claim 77, wherein the vaccine further comprises a low molecular weight chemical irritant or a fragment or a derivative of the chemical irritant.